

We claim:

1. A modified insulinotropic peptide or derivative thereof comprising a reactive group which reacts with amino groups, hydroxyl groups or thiol groups on blood components to form a stable covalent bond.
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2. The peptide of claim 1 wherein said reactive group is selected from the group consisting of succinimidyl and maleimido groups.
- 10 3. A peptide according to claim 2, wherein the derivative is reactive with a thiol group on a blood protein.
4. A peptide according to claim 1 wherein the peptide is selected from the group consisting of SEQ ID NO:2 SEQ ID NO:3, SEQ ID
15 NO:11, SEQ ID NO:13, SEQ ID NO:14 and SEQ ID NO:15.
5. A peptide according to claim 1 wherein the peptide is selected from the group consisting of SEQ ID:16, SEQ ID NO:17, SEQ ID
20 NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21 and SEQ ID NO:22.
6. A composition comprising a derivative of insulinotropic peptide or analog thereof, said derivative comprising a reactive group which reacts with amino groups, hydroxyl groups or thiol groups on blood components
25 to form stable covalent bonds wherein said reactive group is selected from the group consisting of succinimidyl and maleimido groups for use in a method of treating diabetes in a human.
7. The composition of claim 6 wherein said derivative is reactive with
30 blood components.

8. The composition of claim 6 wherein said peptide is selected from the group consisting of SEQ ID NO:2 SEQ ID NO:3, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:14 and SEQ ID NO:15.

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9. The composition of claim 6 wherein said peptide is selected from the group consisting of SEQ ID:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21 and SEQ ID NO:22.

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10. A derivative of an insulintropic peptide, said derivative comprising a maleimido group which reacts with a thiol group on human serum albumin to form a covalent bond.

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11. The derivative of claim 9 wherein said peptide is selected from the group consisting of SEQ ID NO:2 SEQ ID NO:3, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:14 and SEQ ID NO:15.

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12. The derivative of claim 9 wherein said peptide is selected from the group consisting of SEQ ID:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21 and SEQ ID NO:22.

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13. A composition comprising a derivative of an insulinotropic peptide, said derivative comprising a maleimido group which reacts with a thiol group on human serum albumin to form a covalent bond for use in a method of treating diabetes in a human.

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14. The composition of claim 13 wherein the peptide is selected from the group consisting of SEQ ID NO:2 SEQ ID NO:3, SEQ ID

NO:11, SEQ ID NO:13, SEQ ID NO:14 and SEQ ID NO:15.

15. The compositions of claim 13 wherein the peptide is selected from the group consisting of SEQ ID:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21 and SEQ ID NO:22.

16. Use of a composition for the manufacturer of a medicament extending the *in vivo* half-life of an insulinotropic peptide in a diabetes patient the composition comprising a derivative of an insulinotropic peptide or analog thereof, said derivative comprising a reactive group which reacts with amino groups, hydroxyl groups, or thiol groups on blood components to form stable covalent bonds, wherein the reactive group is selected from the group consisting of succinimidyl and maleimido groups.

17. Use of a composition according to claim 16, wherein the derivative is reacted with blood proteins.

18. Use of the composition of claim 16 wherein said peptide is selected from the group consisting of SEQ ID NO:2 SEQ ID NO:3, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:14 and SEQ ID NO:15.

19. An insulinotropic peptide selected from the group consisting of GLP-1(1-36)-Lys³⁷(ε-MPA)-NH², GLP-1(1-36)-Lys³⁷(ε-AEEA-AEEA-MPA)-NH², GLP-1(7-36)-Lys³⁷(ε-MPA)-NH², GLP-1(7-36)-Lys³⁷(ε-AEEA-AEEA-MPA)-NH², D-Ala² GLP-1(7-36)-Lys³⁷(ε-MPA)-NH², D-Ala² GLP-1(7-36)-Lys³⁷(ε-AEEA-AEEA-MPA)-NH², exendin-4 (1-39)-Lys⁴⁰(ε-MPA)-NH², exendin-4(1-39)-Lys⁴⁰(ε-AEEA-AEEA-MPA)-NH², exendin-3(1-39)-Lys⁴⁰(ε-MPA)-NH² and exendin-3(1-39)-Lys⁴⁰(ε-AEEA-AEEA-

MPA).